M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: February 7, 2000

To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: Update on the Office of Generic Drugs

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation:	Update on the Office of Generic Drugs
Presented for:	National Pharmaceutical Alliance Fall Meeting
Date Presented:	10/7/98
Presented by:	Douglas L. Sporn
Number of Pages:	57

M. Lamb

Attachment

90S-0308

M647

National Pharmaceutical Alliance Fall Meeting

Update on the Office of Generic Drugs

Douglas L. Sporn
Director
Office of Generic Drugs
Las Vegas, Nevada
October 7, 1998

Update on the Office of Generic Drugs

- Staffing & Recruitment
- Trends
- Challenges
- 180 Day Exclusivity
- Guidance Development
- Electronic Submissions

Recent Hires/Selections

- Barbara Davit, Ph.D., Team Leader, Bioequivalence
- Pat Beers-Block, Team Leader, Label. & Program Supp.
- Four Bioequivalence Reviewers
- Statistician
- Computer Specialist
- Labeling Reviewer
- Microbiologist

Recruitment

- 1 Microbiologist Team Leader
- 4 Chemistry Reviewers
- 1 Project Manager to support Bioequivalence
- 1 Project Manager to support Chemistry

Note: Includes recruitment efforts above ceiling.

Project Managers for Bioequivalence

Former Staff:

Lizzie Sanchez to Spec. Asst. Bioequivalence

Nancy Chamberlin to Office of Rev. Management

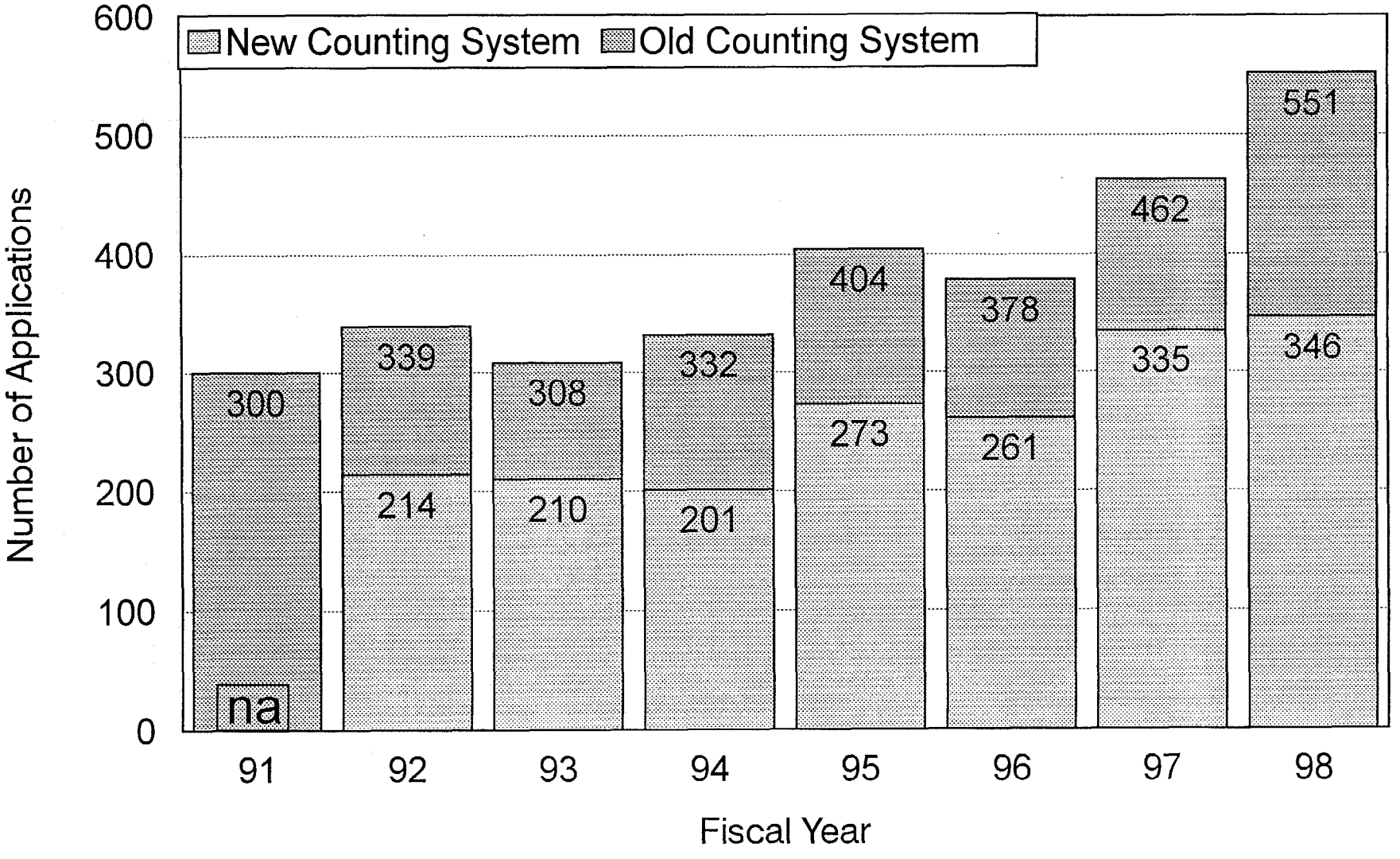
New Staff:

Nassar Mahmud from Regulatory Support Branch

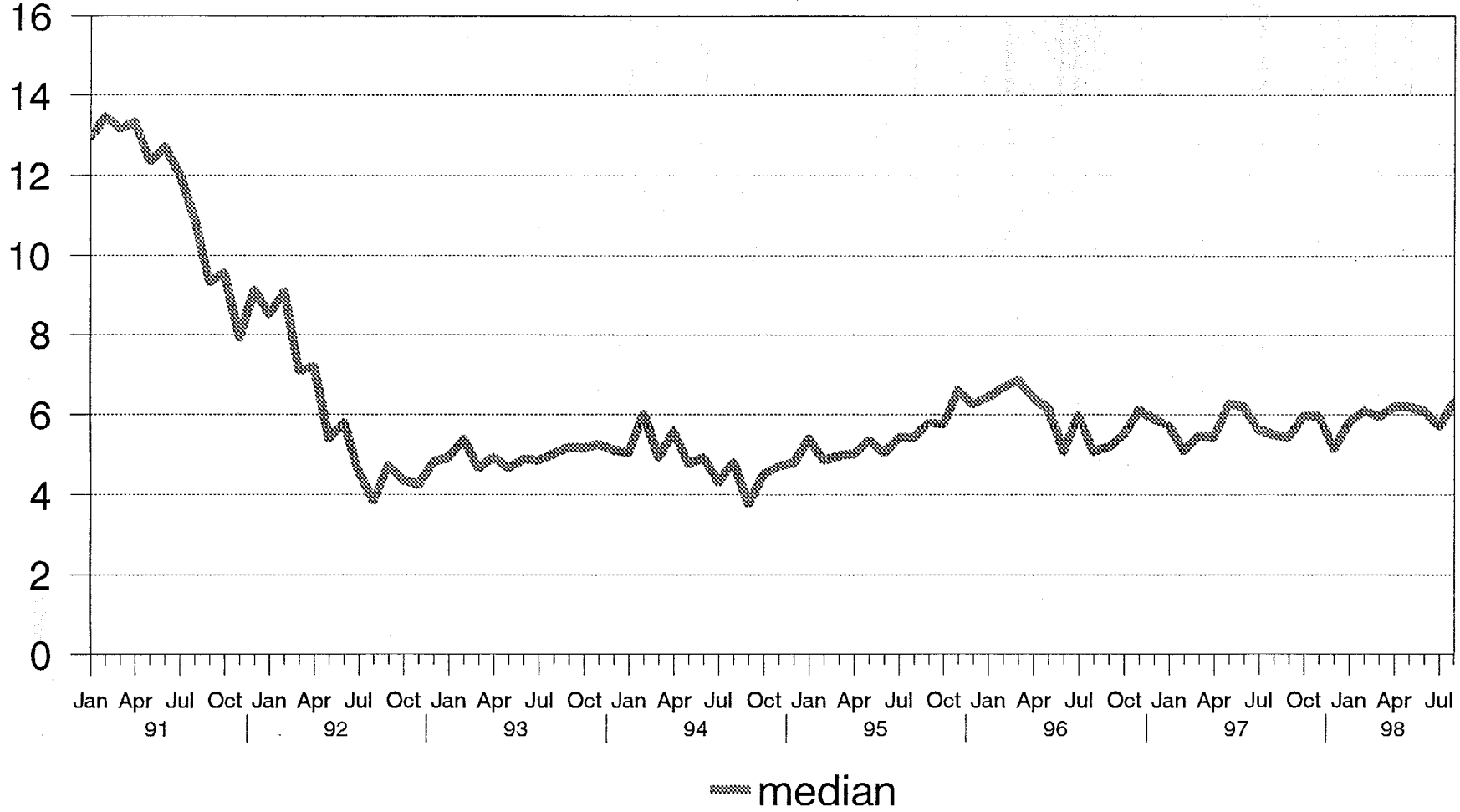
Elaine Hu

3rd Project Manager being recruited

Fiscal Year Receipts



Median ANDA Review Cycle (Months) (Original Applications)



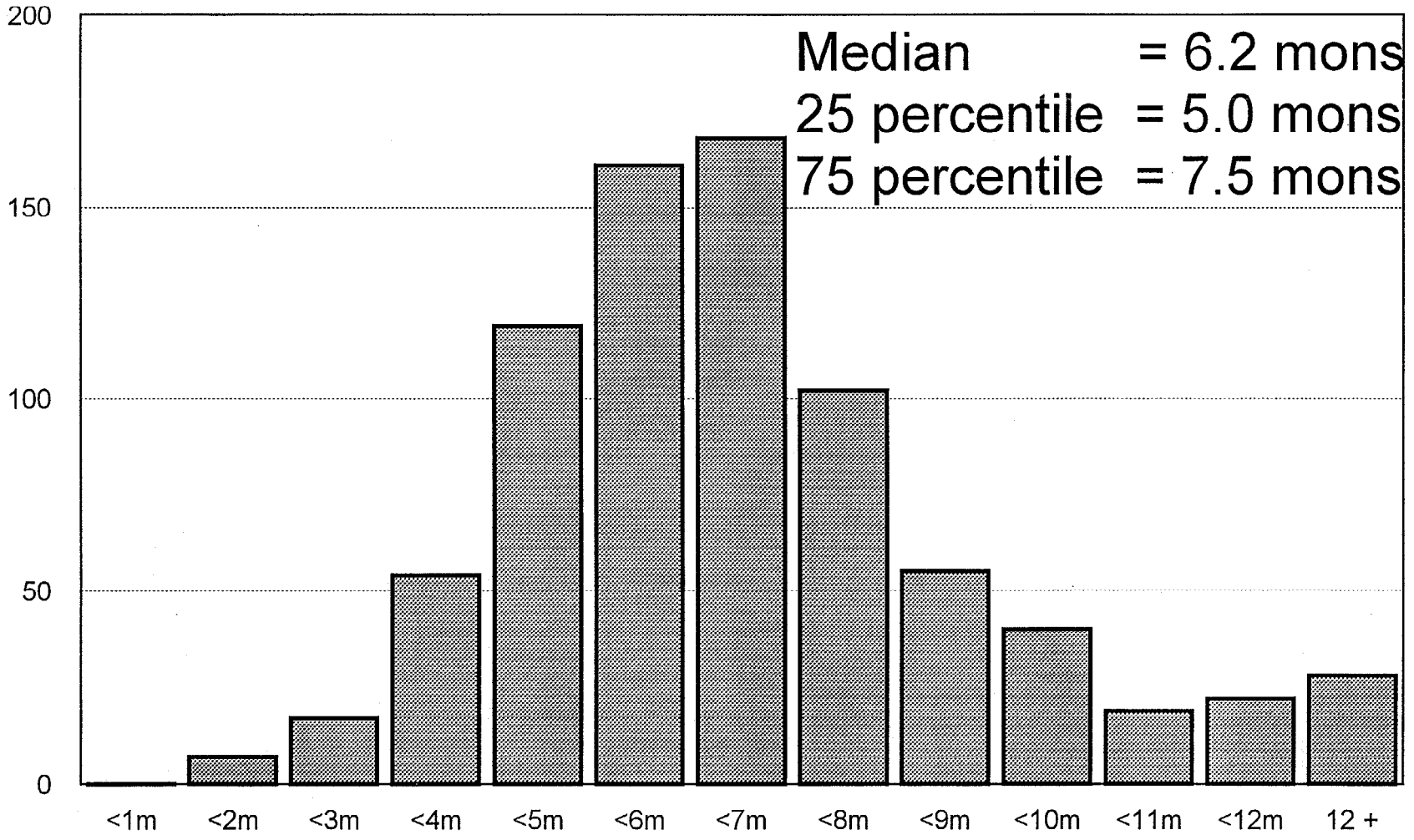
1-Times correspond to actual applications received . The new ANDA/AADA submission policy that went into effect 1/1/91 allows certain variations in a drug product to be included in a single application.

2-In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. AIP time has been subtracted from review time above for the period after 9/91. However, before the AIP went into effect, the review of many applications suspected of containing fraudulent data were suspended. These suspensions were not recorded in the MIS and are not reflected in the above chart.

x:\hg_files\monthly\stats.prs

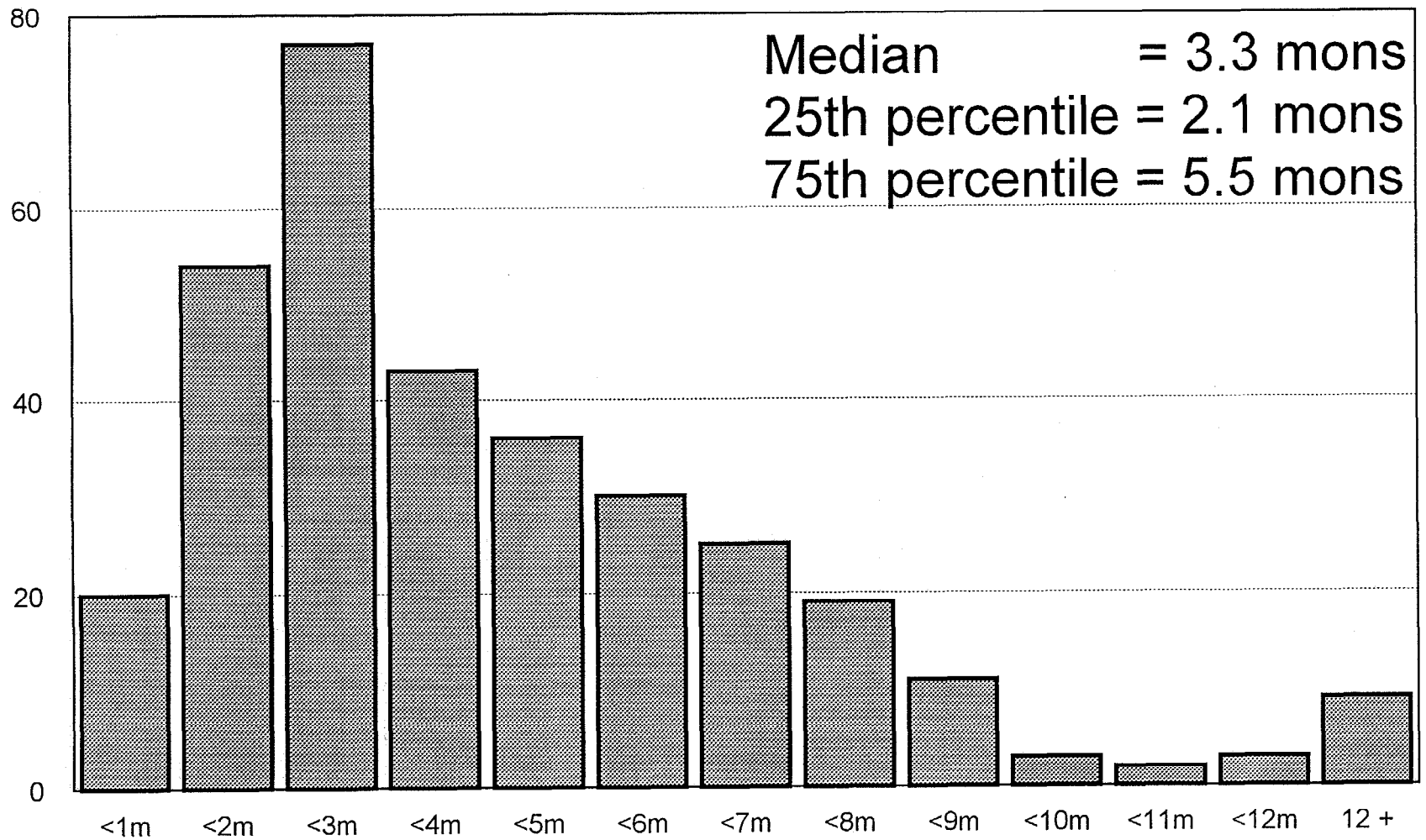
Distribution of Review Times for Original ANDAs

Major Cycles Only--1/1/97--6/30/98

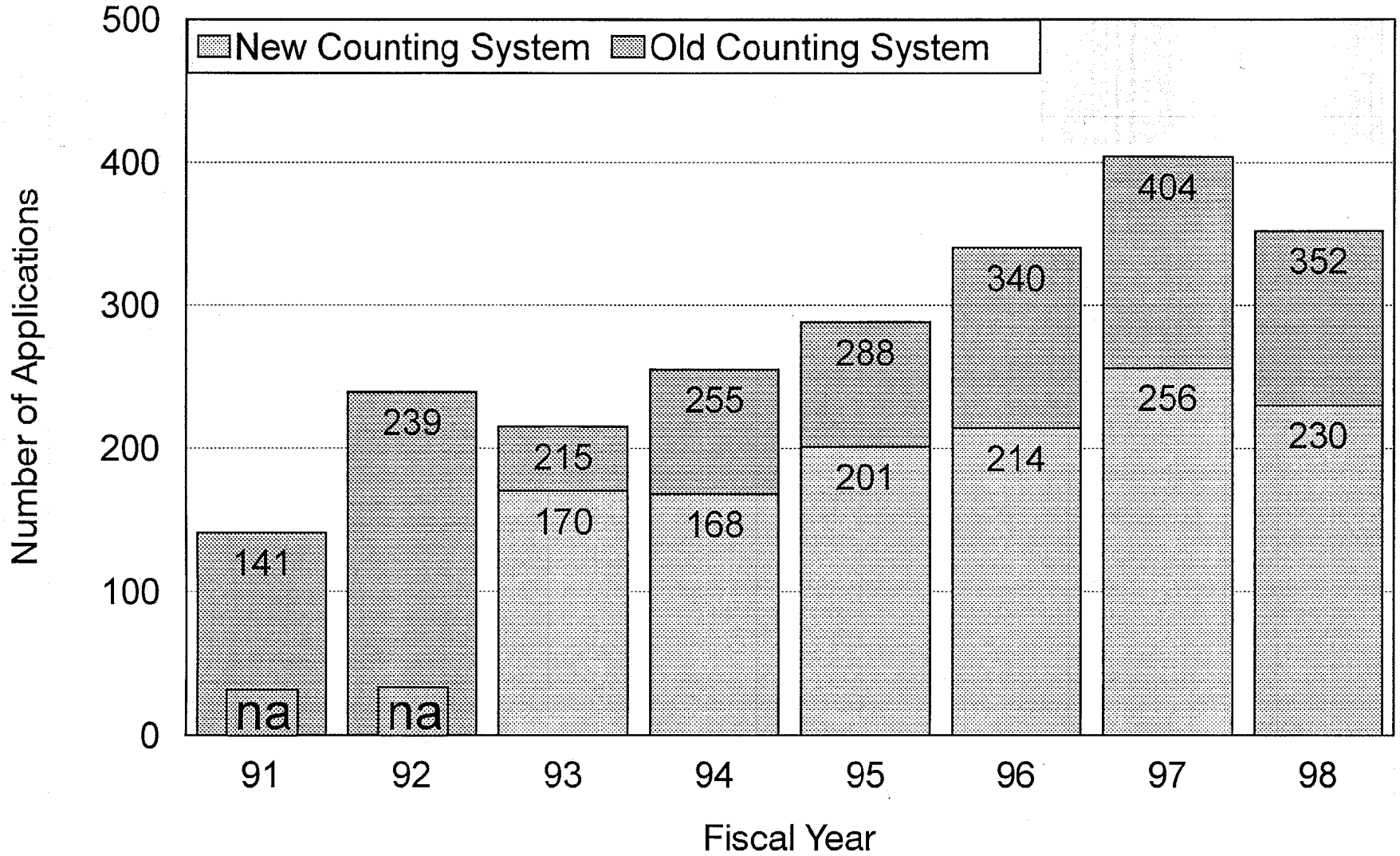


Distribution of Review Times for Original ANDAs

Minor Cycles Only--1/1/97--6/30/98



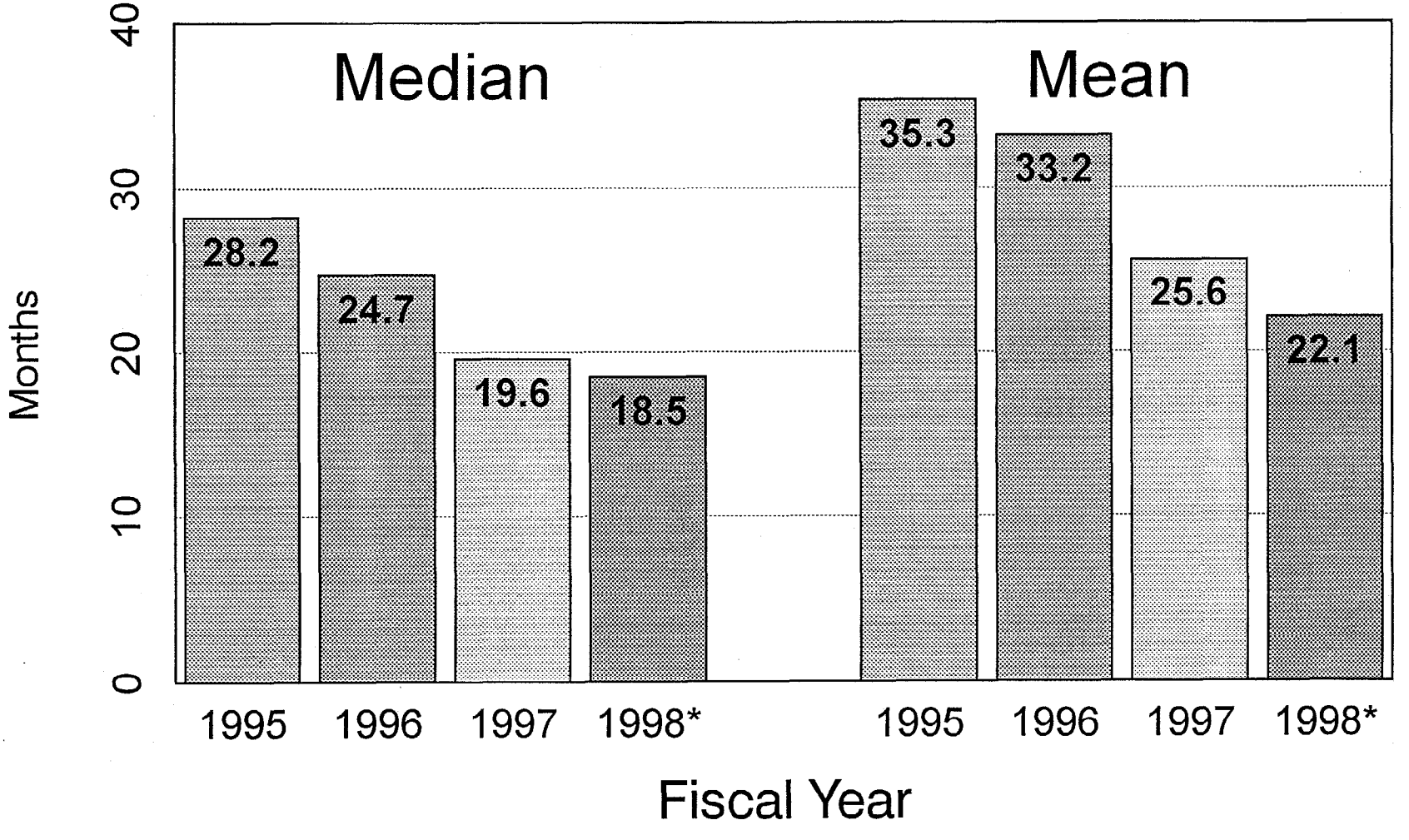
Fiscal Year Approvals



Possible Reasons for Fewer Approvals

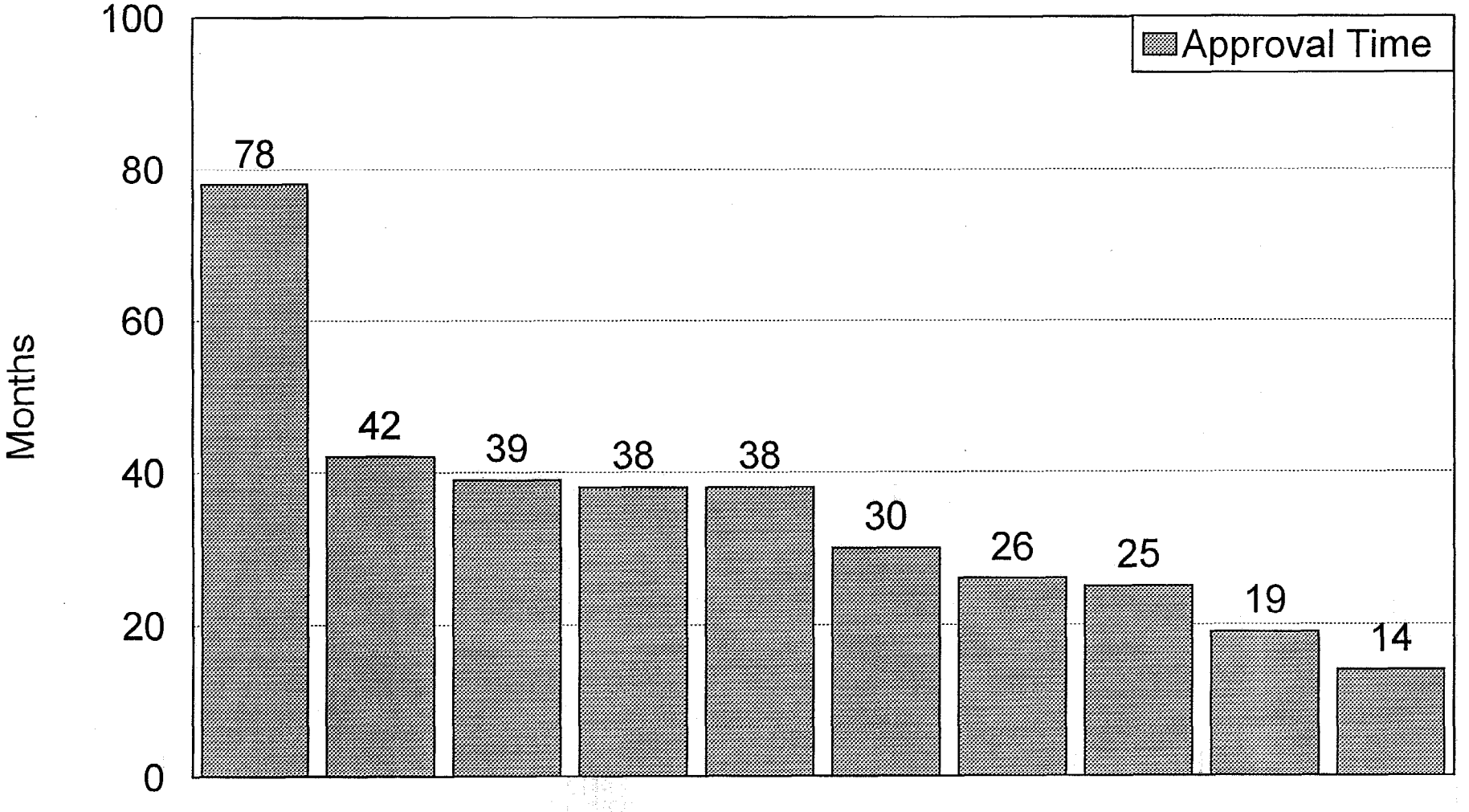
- Turn over in staff & recruiting/training new staff
- Reviewer time conflicts
  - Citizen Petitions & Grumps
  - Guidances
  - Controlled Correspondence
  - Mentoring
- Impact of ANDA exclusivity
- Bulk AADA's are no longer being approved

Approval Times

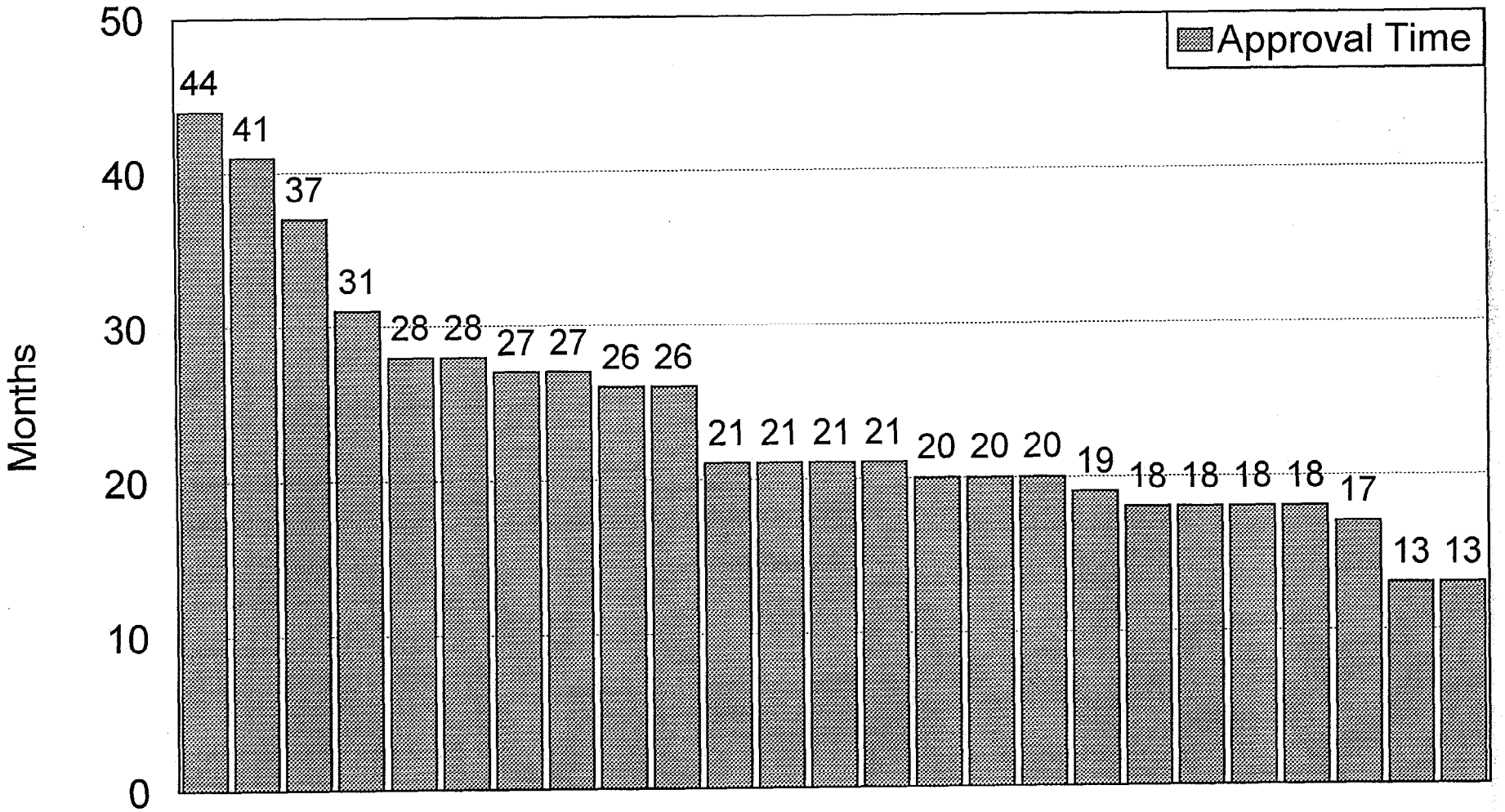


* = Through August 30, 1998

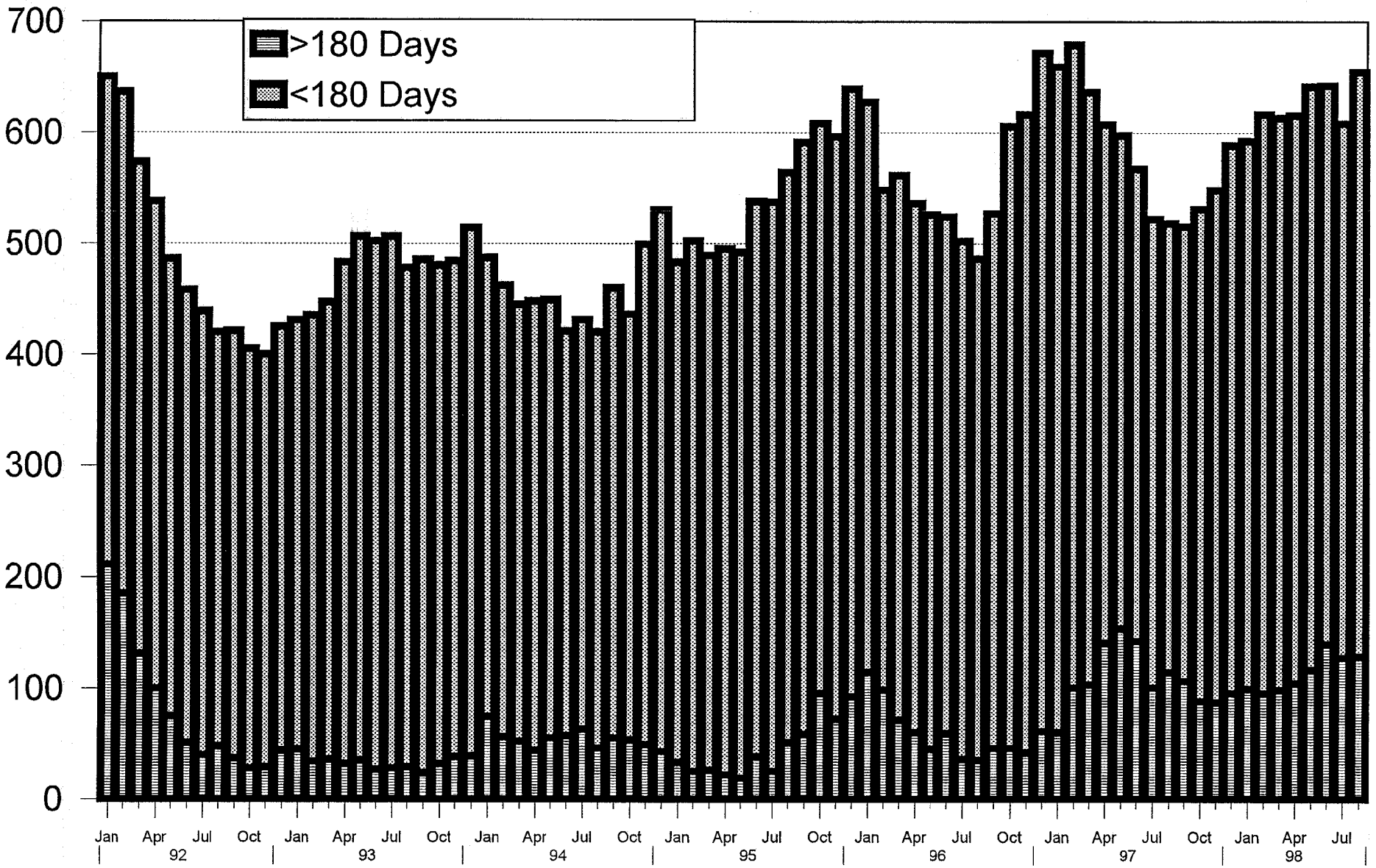
ANDA Approvals Summary for Ranitidine (Solid Oral Dosage Forms)



ANDA Approvals Summary for Cimetidine (Solid Oral Dosage Forms)

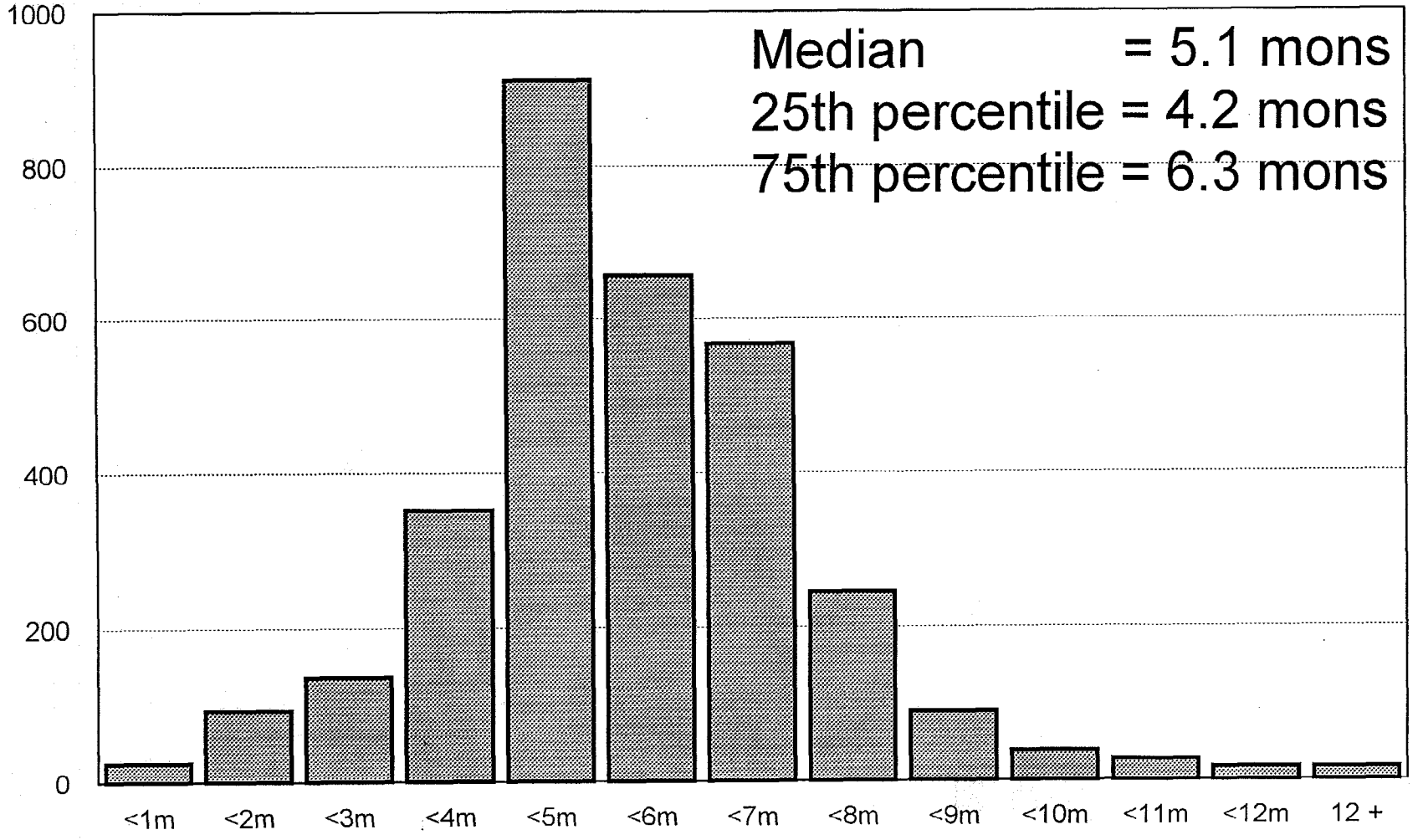


Original ANDAs Pending Per Month



Distribution of Review Times for Manufacturing Supplements

Major Cycles Only--1/1/97--6/30/98



Distribution of Review Times for Manufacturing Supplements

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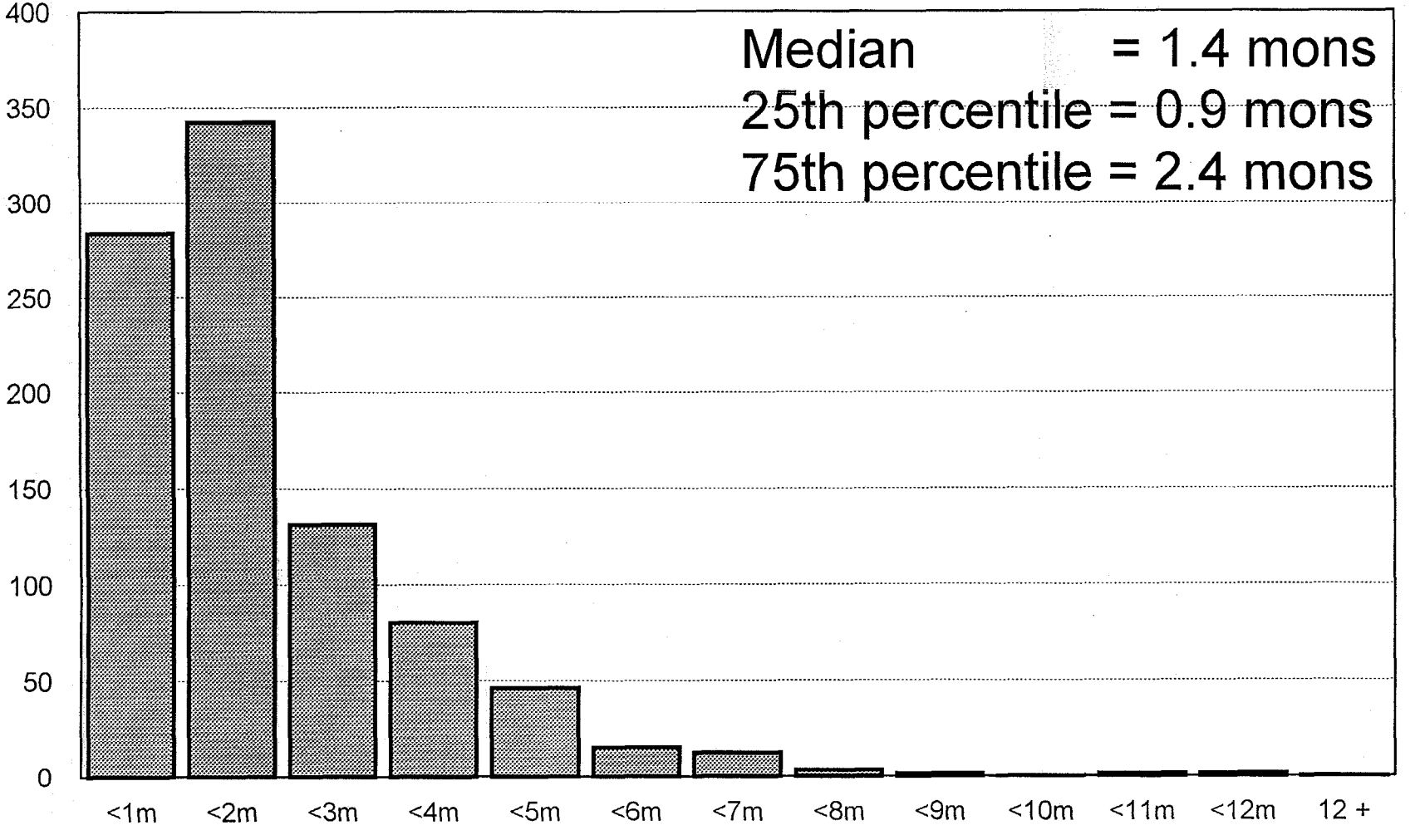

Challenges
(OGD is involved with)

Type	Total	Science	Patent & Exclusivity
Citizen Petitions	22	16	6
Law Suits	8	2	6
"Grumps"	13	11	2

180 Day Generic Drug Exclusivity Guidance

- How FDA is applying exclusivity provision of the Act in light of recent court decisions
- FDA's "litigation" and "successful defense" requirements for exclusivity challenged
  - Inwood Labs
  - Mova
  - Granutec
- FDA will not appeal Court of Appeals' rulings.

180 Day Generic Drug Exclusivity Guidance (cont.)

- Remove "successful defense" provisions from 314.107(c)(1) to be followed by rule making for new regulations
- Until rule making is complete, FDA will regulate directly from statute and make decisions on exclusivity on a case-by-case basis
- First to file with Paragraph IV and even if <u>not</u> sued is entitled to 180 day exclusivity

Guidance for Industry:
180 Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments to the FD&C Act

Internet:

http://www.fda.gov/cder/guidance/index.htm

Chemistry and Manufacturing Controls Guidances in Development

- 314.70 Revisions (FDAMA)
- Stability
- Impurities in Drug Substance
- Impurities in Drug Product
- Packaging
- MDI's (Metered Dose Inhalers) & DPI's (Dry Powder Inhalers)

Chemistry and Manufacturing Controls Guidances in Development (cont.)

- PACSAS (Sterile Aqueous Solutions)
- *Draft* SUPAC-IR/MR Equipment Addendum
- *Draft* SUPAC-SS Equipment Addendum
- BACPAC I & II

Bioequivalence Guidances in Development

- Bioavailability and Bioequivalence Studies for NDAs and ANDAs: Orally Administered Drug Products
- *In Vivo* Bioequivalence Studies Based on Population and Individual Bioequivalence Approaches
- Food Effect Bioavailability and Bioequivalence Studies
- Topical Dermatological Product NDAs and ANDAs - *In Vivo* BA, BE, *In Vitro* Release and Associated Statistics
- Biopharmaceutics Classification System

Bioequivalence Guidances in Development

- *In Vivo* Bioequivalence Studies Based on Population and Individual Bioequivalence Approaches
- Food Effect Bioavailability and Bioequivalence Studies
- Topical Dermatological Product NDAs and ANDAs - *In Vivo* BA, BE, *In Vitro* Release and Associated Statistics
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OGD Guidances in Development

- Content and Format of an ANDA
- Variations in Dosage Forms that can be Submitted Within a Single ANDA
- Blend Uniformity Analysis
- Policy on Identification of Major, Minor, and Facsimile Amendments to Original ANDA's

Electronic Submissions Status:

- Bio: 11 companies with 23 submissions
- CMC: 8 companies with 13 submissions
  (Included are 6 companies submitting a submission with both Bio and CMC elements)
- Electronic Submissions Working Group with Generic Trades
- Working on improving EVA based on user feedback
- Plant visitations held
- Richard Sponaugle selected

Electronic Submissions

Points to Consider:

- 45 day grace period for electronic submission receipt after hard copy receipt

- Attend training with U. of MD (BE &/or CMC)

- Include declaration of hard copy and electronic submission as identical (between applicant and FDA)

- Address questions to OGD :
  - General: Ruth Warzala 301-827-5845
  - BE: Kharidia Jahravi 301-827-5847
  - CMC: Jon Clark 301-827-5849

Electronic Submissions

Check the Web site for information on ANDA submissions:

Mundos.ifsm.umbc.edu/~fdacom

Background

Document Room

Staff: 12 on-board
(contractors only)

Cost: $440,000

(There is currently 1 liaison *CDER* FTE)

Chemistry and Manufacturing Controls Guidances in Development

- 314.70 Revisions - *Proposal being drafted*
- Stability - *Extended comment period ends 12/8/98*
- Impurities in Drug Substance - *Published any day (if not already) with 60 comment period*
- Impurities in Drug Product - *with RPS for editing*
- Packaging - *Being revised by Committee, needs CMC CC and RPS clearance after.*
- MDI's (Metered Dose Inhalers) & DPI's (Dry Powder Inhalers) *- still being worked on per Patel*

Chemistry and Manufacturing Controls Guidances in Development (cont.)

- PACSAS (Sterile Aqueous Solutions)
  - *Being drafted*

- *Draft* SUPAC-IR/MR Equipment Addendum
  - *being worked on*

- *Draft* SUPAC-SS Equipment Addendum
  - *being worked on per Patel*

- BACPAC I & II
  I = with RPS/Axelrad for review
  II = being drafted

Joe B. Project

Assistance to Applicants

- Initiative: Offer assistance/teleconference to applicants receiving multiple not approvable letters.

- Goal: Reduce approval time by increasing communication.

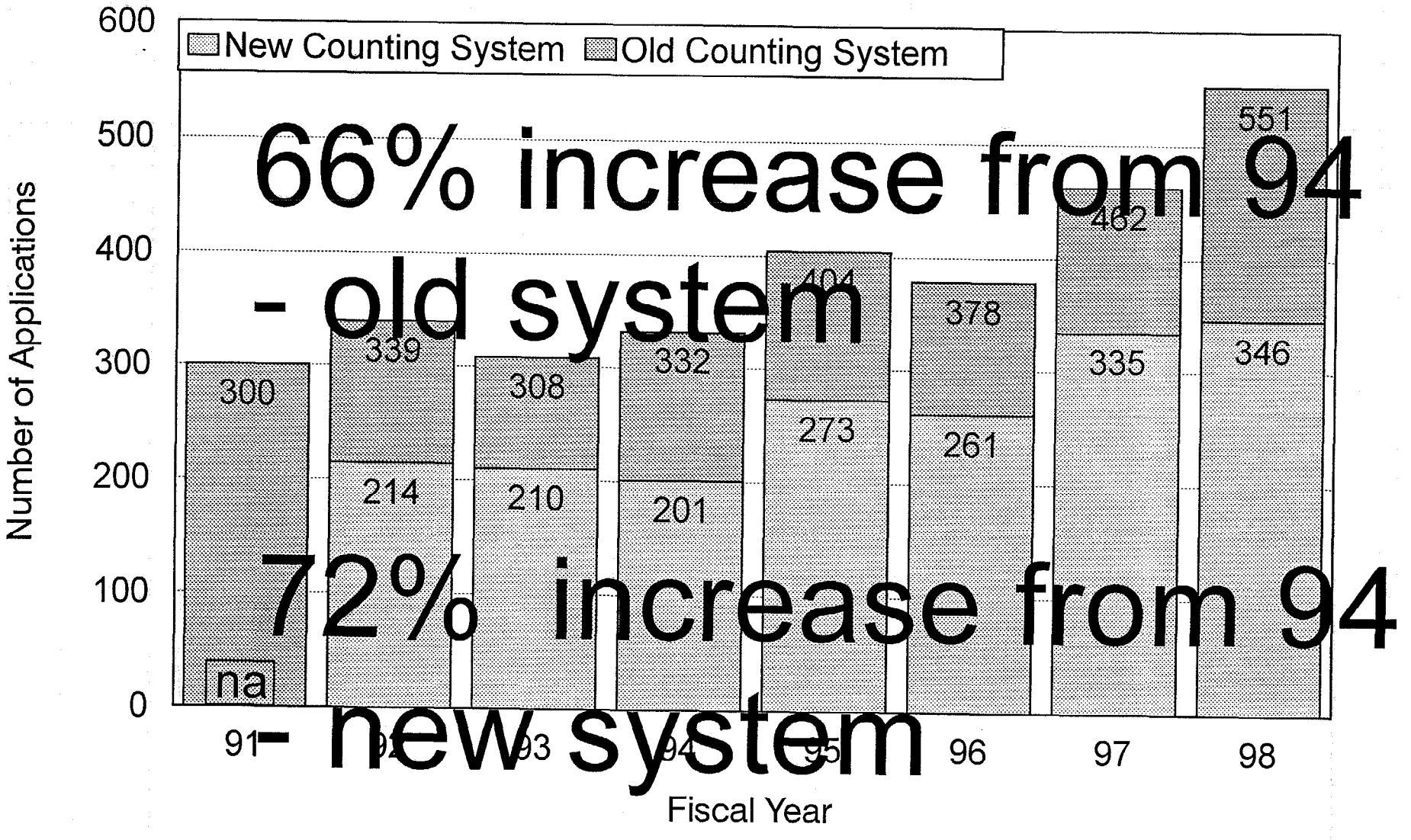
- Status: After two year's experience it is clear that firms communicating with OGD are more likely to be approved, and the approval times are reduced.

Other News

- Faxing DMF deficiencies to the DMF holder (or their U.S. agent)

Documentation ready mid-Oct 98 per Pat B2

Fiscal Year Receipts



Bioequivalence Guidances in Development

- Bioavailability and Bioequivalence Studies for NDAs and ANDAs: Orally Administered Drug Products - *Also called General Guidance.Final with RPS for clearance per Shah. Cory chart says issue 11/99.*

- *In Vivo* Bioequivalence Studies Based on Population and Individual Bioequivalence Approaches - *Draft issued, comment period closed, two year "trial period" begins with issuance of "General Guidance." Will be discussed at 10-9-98 Expert Mtg (Public) and 10-22-98 Advisory Committee.per Shah*

- Food Effect Bioavailability and Bioequivalence Studies - *Final with RPS for clearance.per Shah*

- Topical Dermatological Product NDAs and ANDAs - *In Vivo* BA, BE, *In Vitro* Release and Associated Statistics - *Draft out. Will be discussed at 10-23-98 OPS/Derm Advisory Committee. Final out by 1-1-99. per Shah.*

- Biopharmaceutics Classification System - *Draft on hold with RPS. per Shah.*

Recent Hires/Selections

- Barbara Davit, Ph.D., Team Leader, Bioequivalence
  - May 98 Start Date
- Pat Beers-Block, Team Leader, Label. & Program Supp.
  - March 98 Start Date
- Four Bioequivalence Reviewers
- Statistician
- Computer Specialist
- Labeling Reviewer
- Microbiologist

Notable *Scientific* Challenges

(Citizen Petitions & Law Suits)

Amiodarone
Cyclosporine
Diltiazem
Estradiol
Iopamidol
Menotropins
Nifedipine
Propofol
Selegiline
Verapamil

Notable *Patent & Exclusivity* Challenges

(Citizen Petitions & Law Suits)

Glyburide
Hydroxyurea
Nabumetone
Tamoxifen
Terfenadine
Terazosin
Ticlopidine

Ranitidine (Solid Oral Dosage Forms)

Survey Size: 10

	Approval Times Months	Number of Reviews
Range:	14-78	2-6
Mean:	35	4
Median:	34	4
Mode:	38	4

Cimetidine (Solid Oral Dosage Forms)

Survey Size: 25

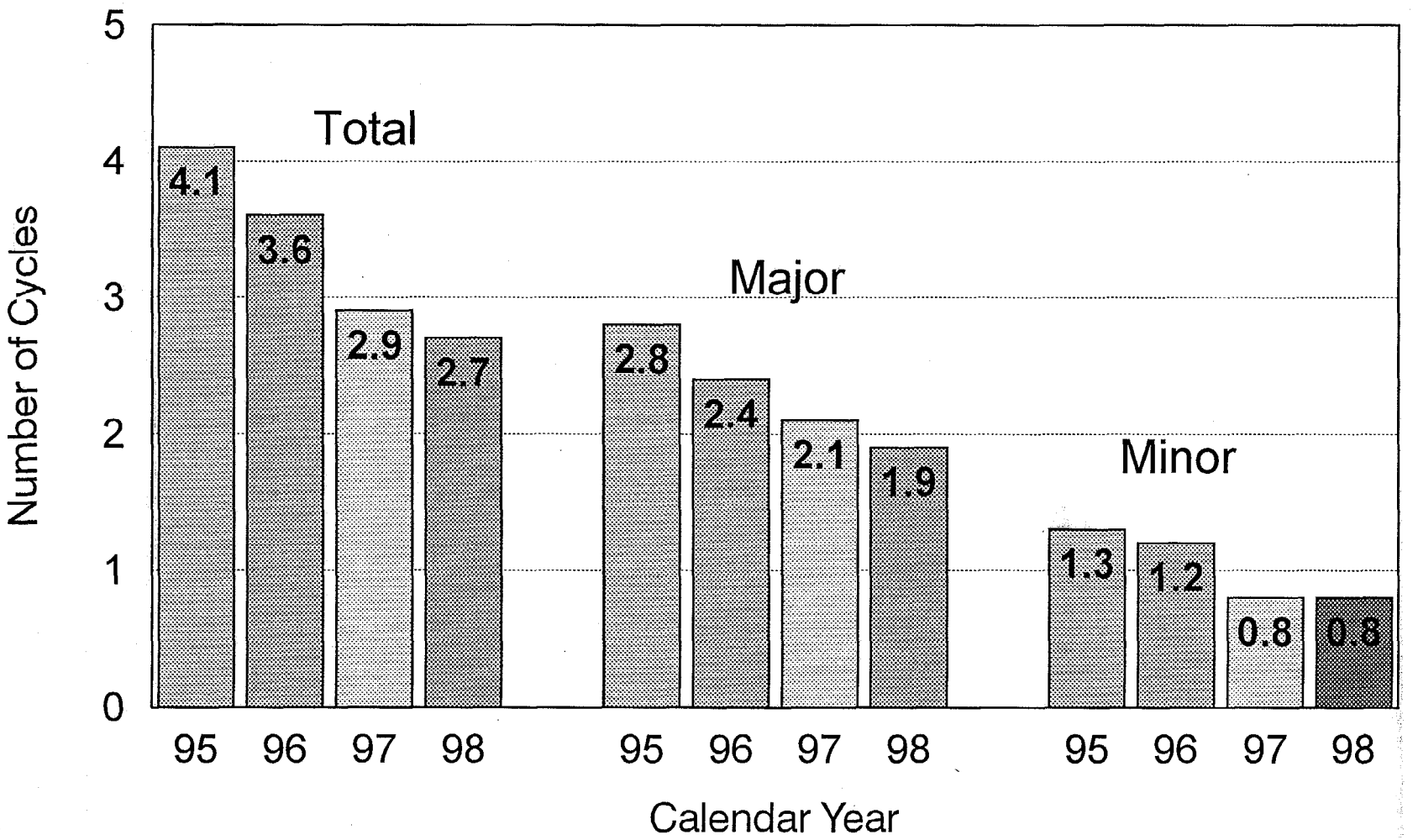
	Approval Times Months	Number of Reviews
Range:	13-44	2-5
Mean:	24	3.3
Median:	21	3
Mode:	21	3

Cimetidine (Solutions)

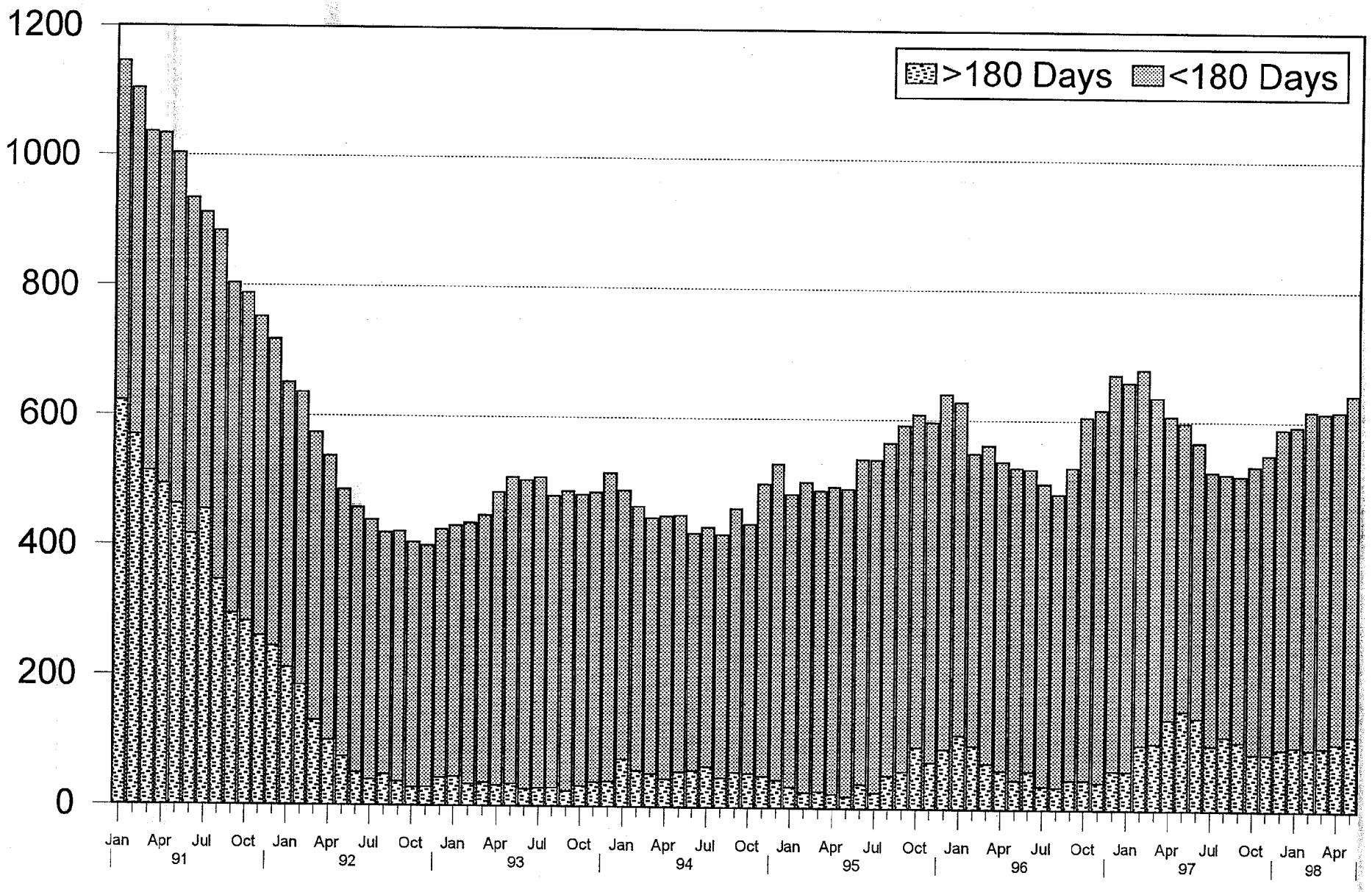
Survey Size: 9

	Approval Times Months	Number of Reviews
Range:	14-35	3-5
Mean:	25.6	3.6
Median:	27	3
Mode:	27	3

Number of Review Cycles



ANDAs Pending Per Month

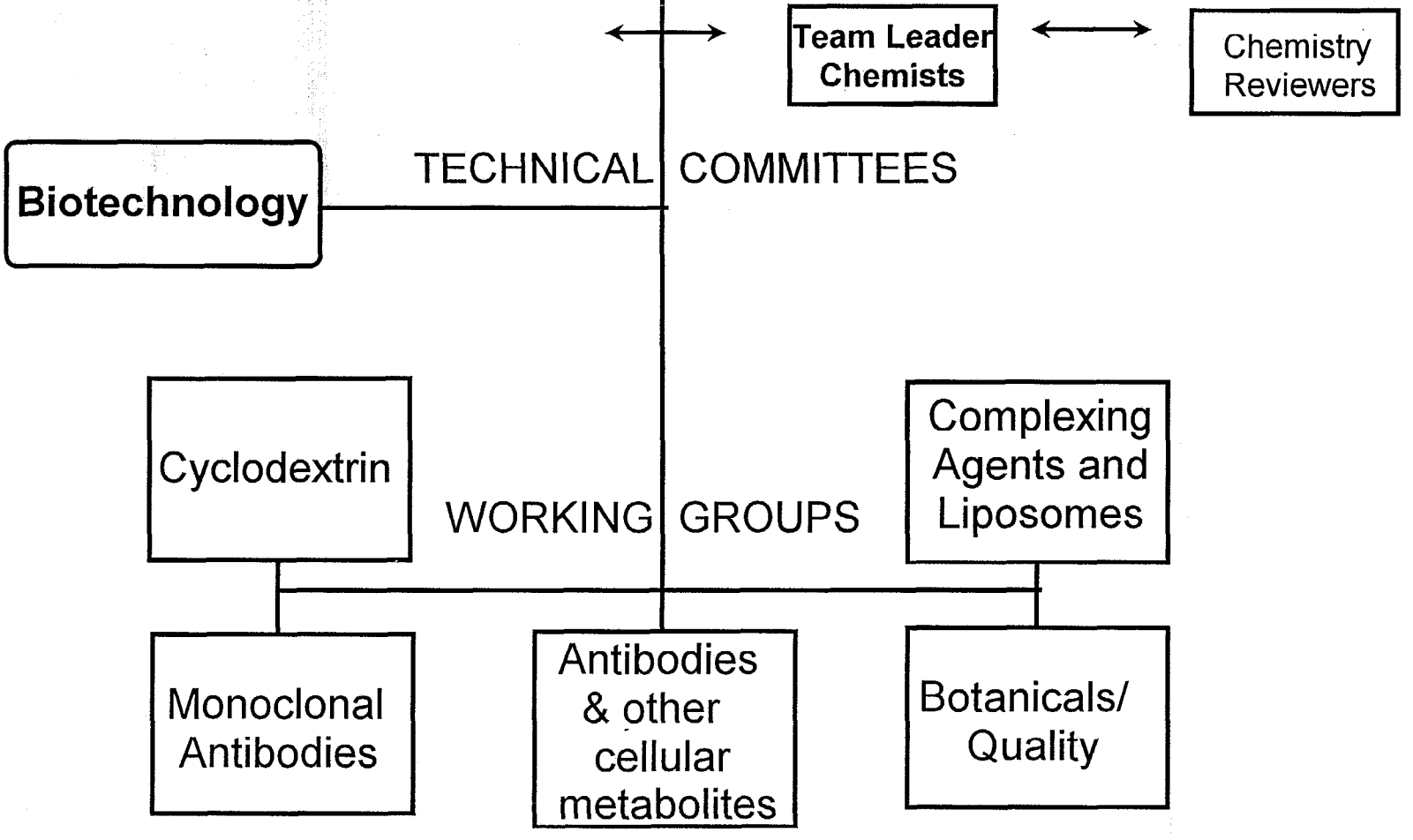


DRAFT

Complex Drug Substances Coordinating Committee

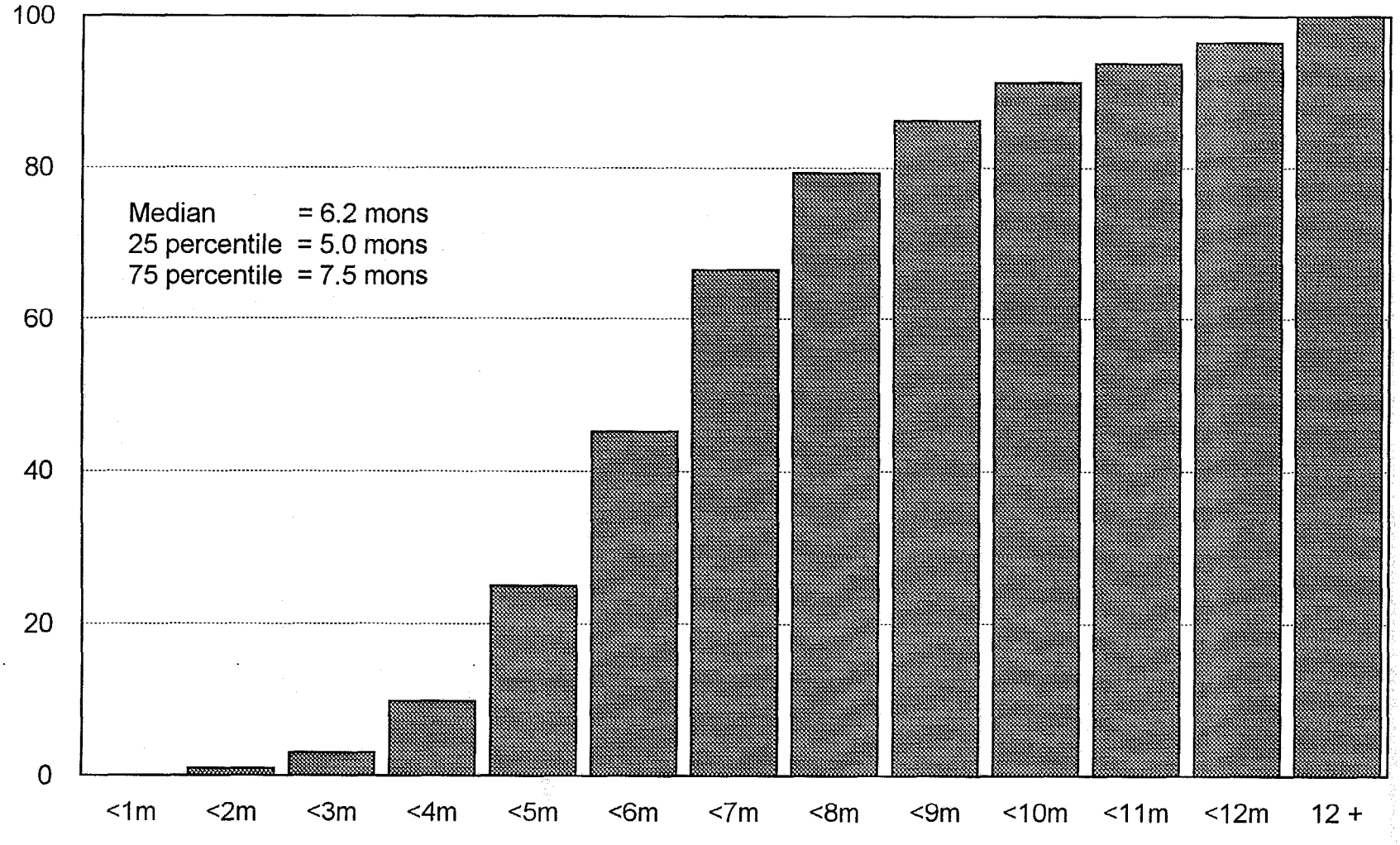
Dr. Williams, Dr. Chiu, R. Hassall

DRAFT



Cumulative Distribution of Review Times for Original ANDAs

Major Cycles Only--1/1/97--6/30/98



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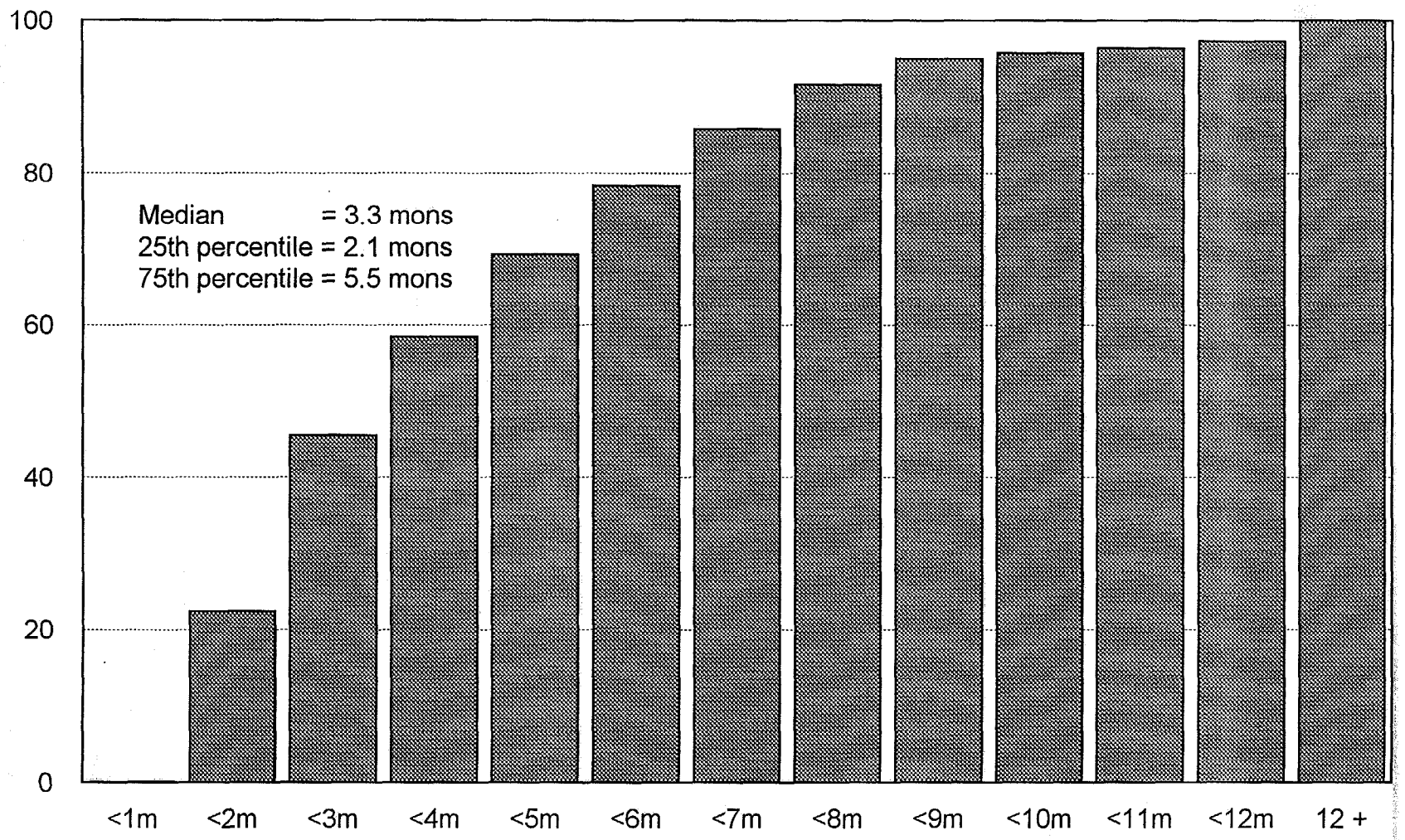
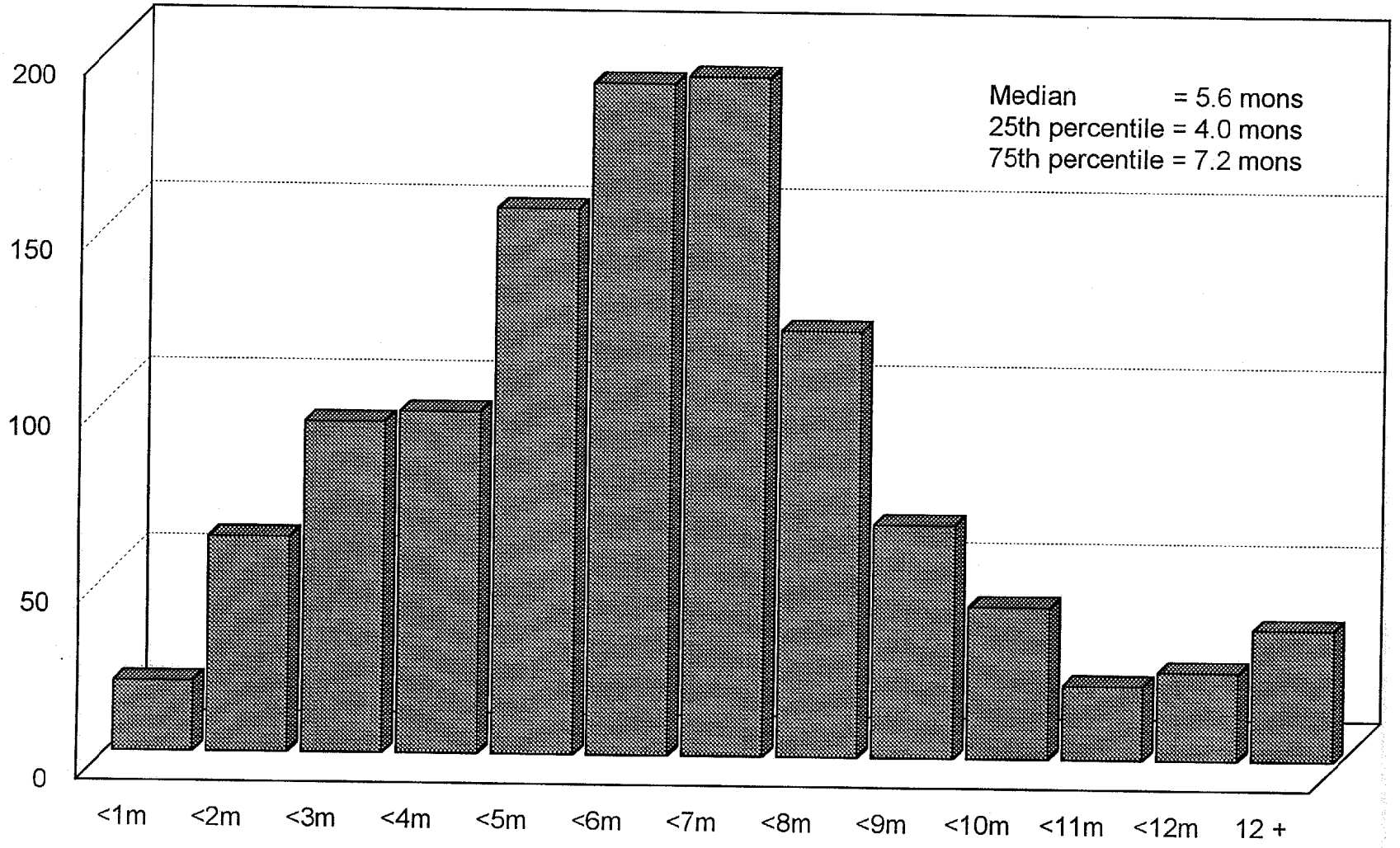


Distribution of REview Times for Original ANDAs

Major and Minor Cycles--1/1/97--6/30/98



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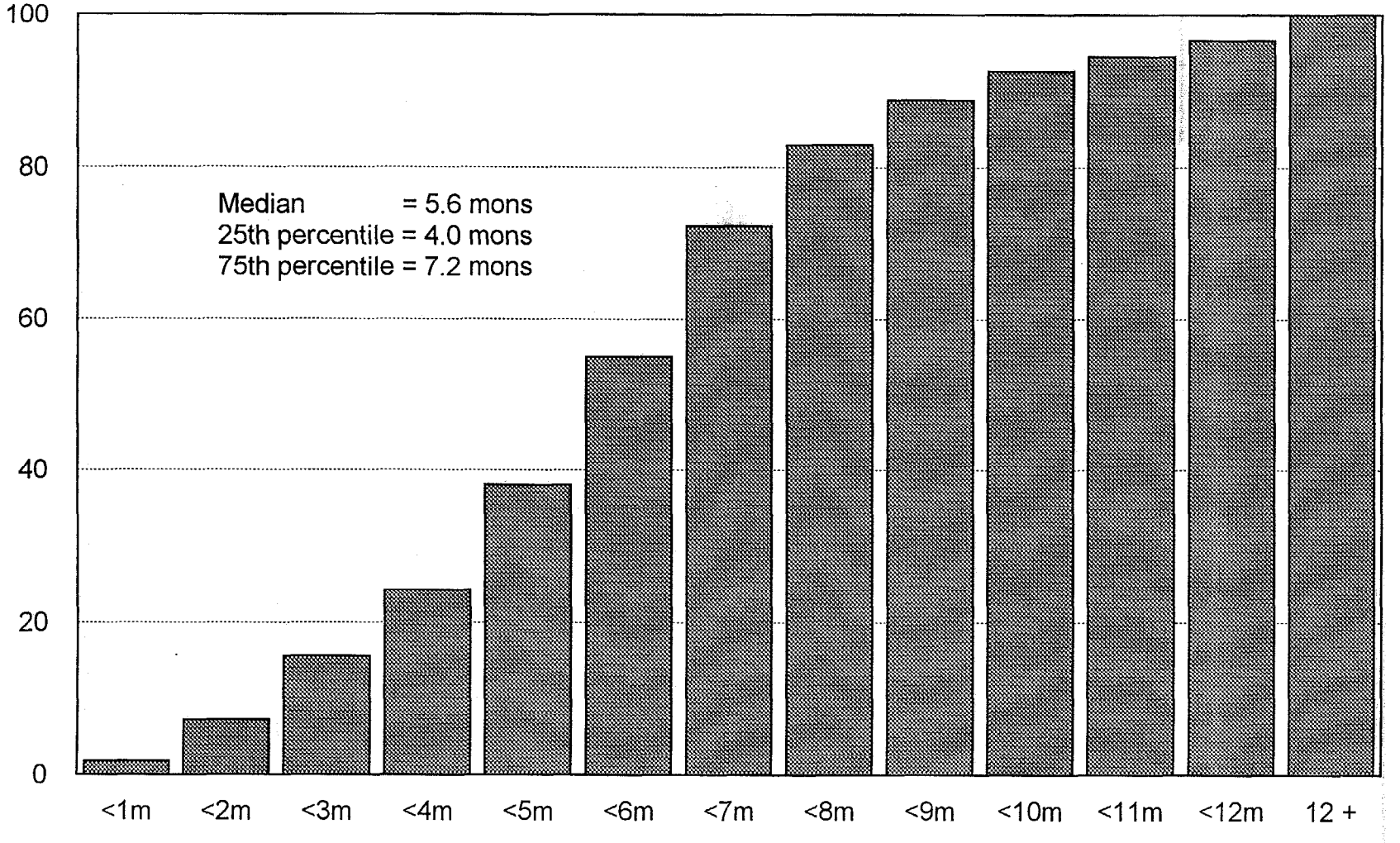

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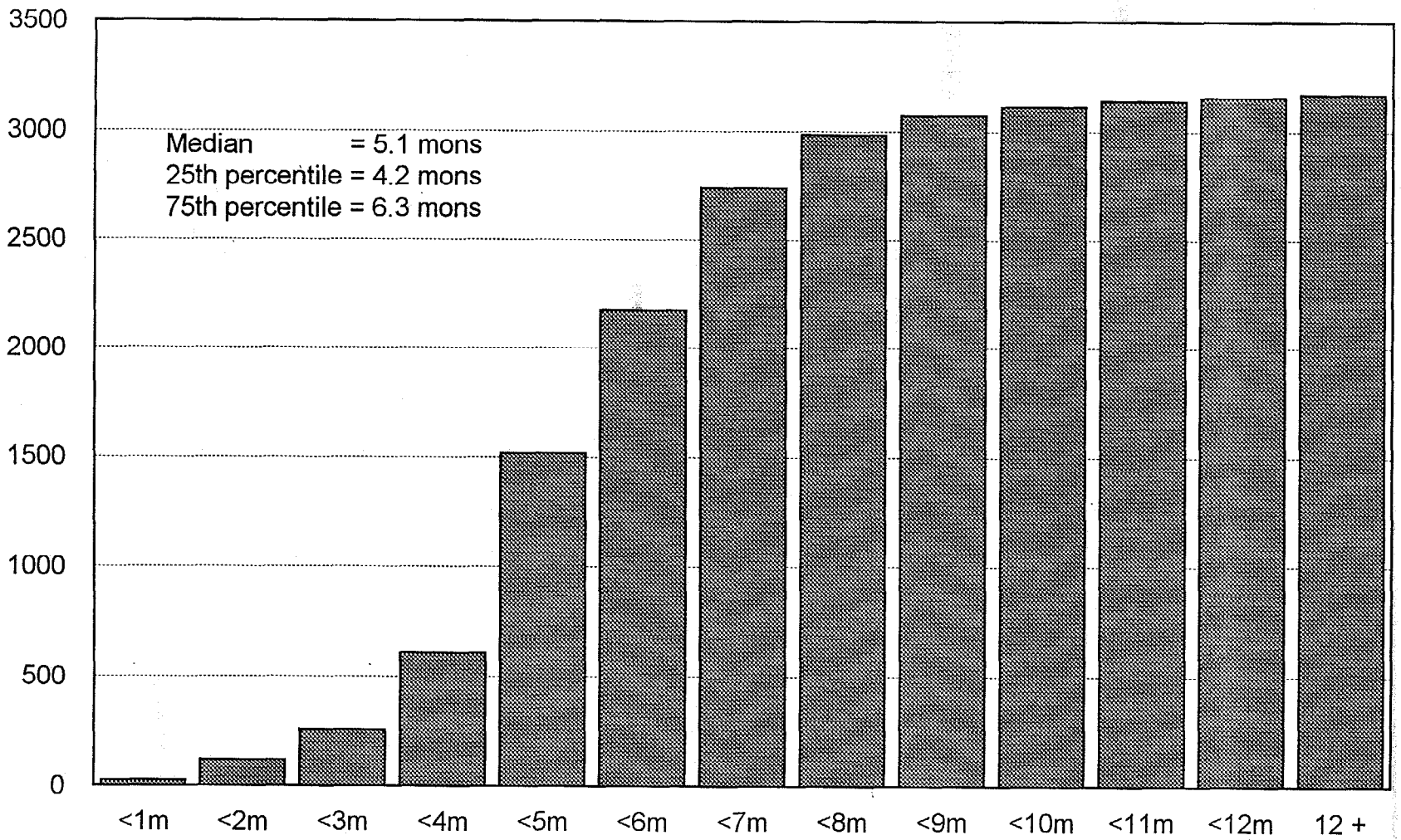

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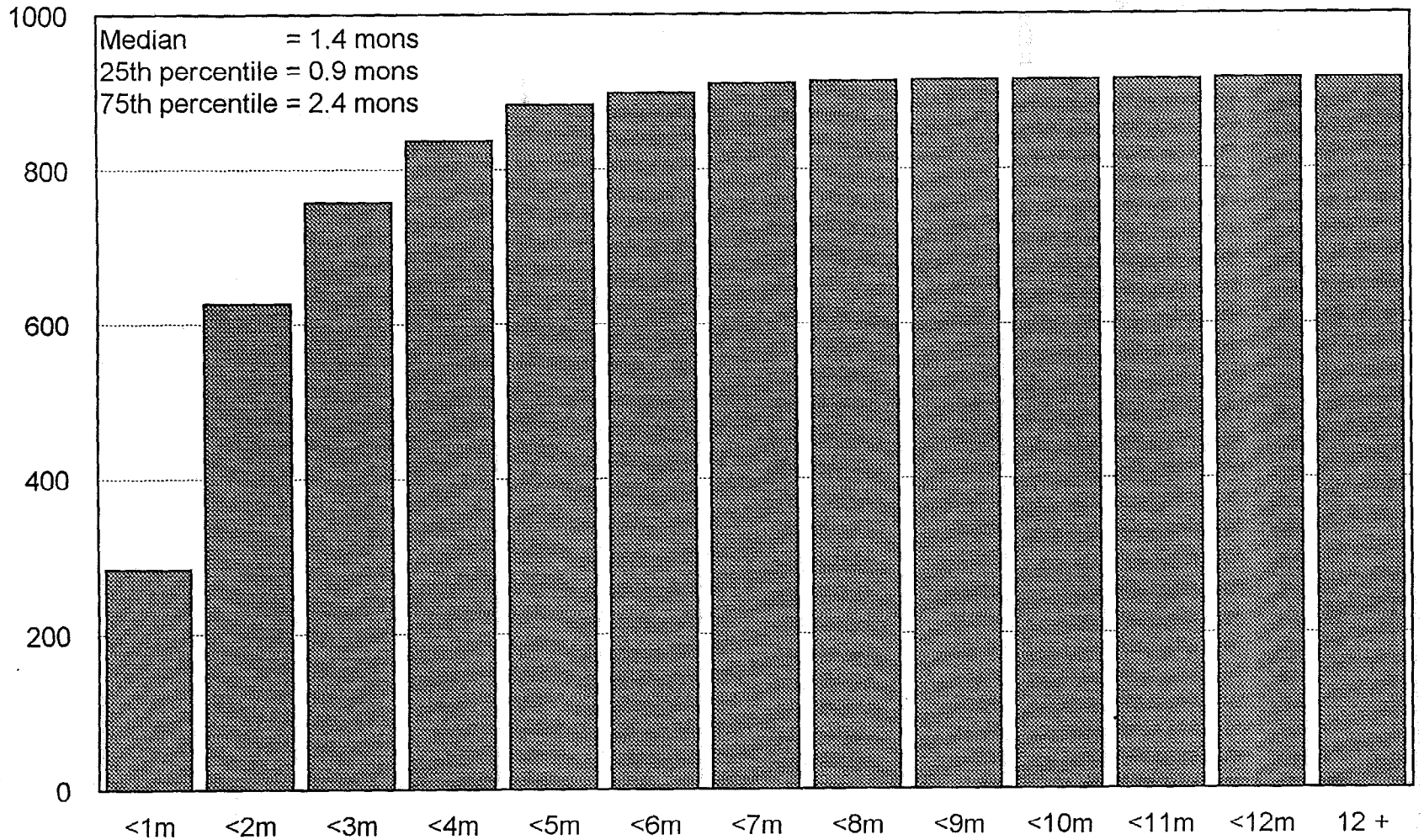

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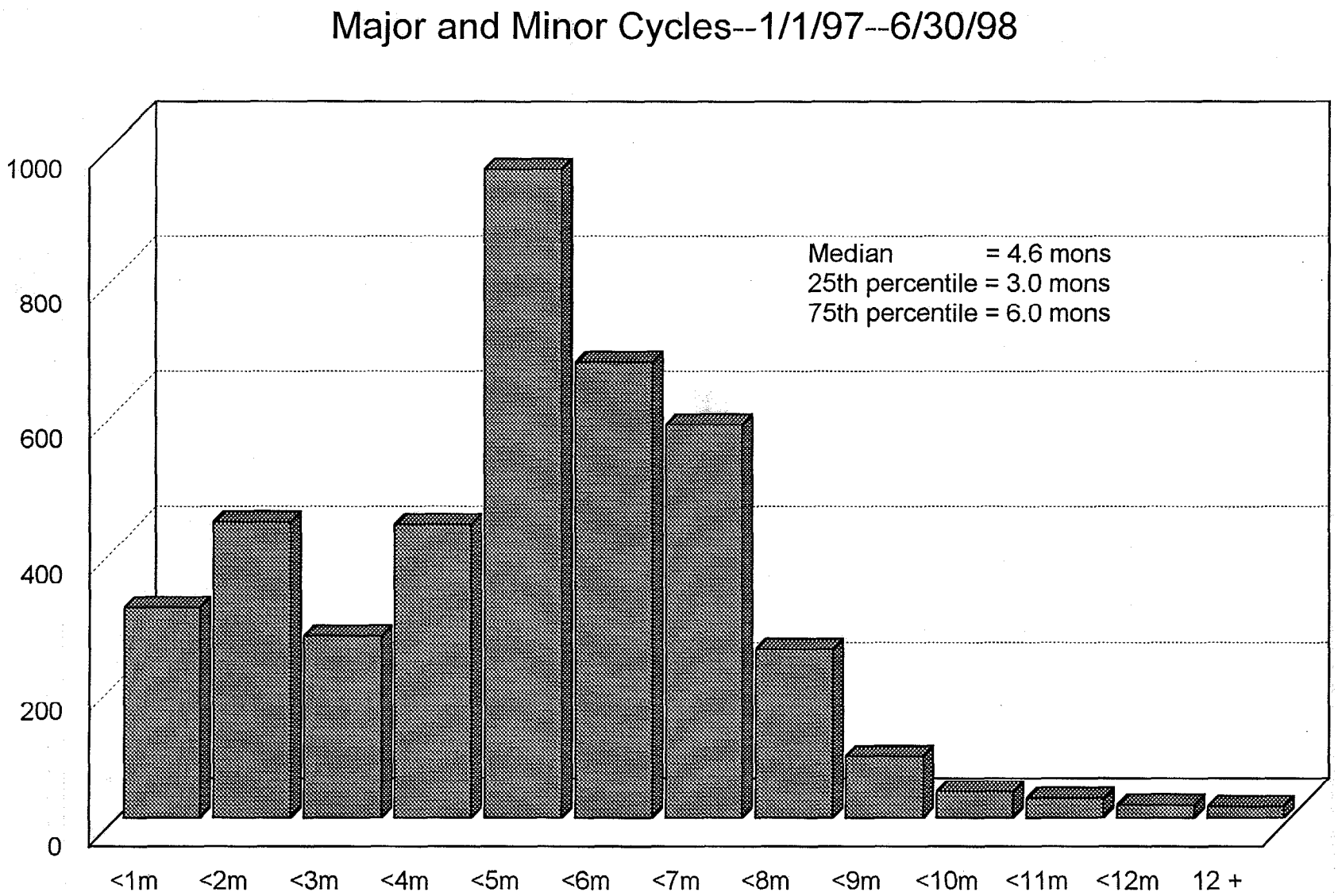

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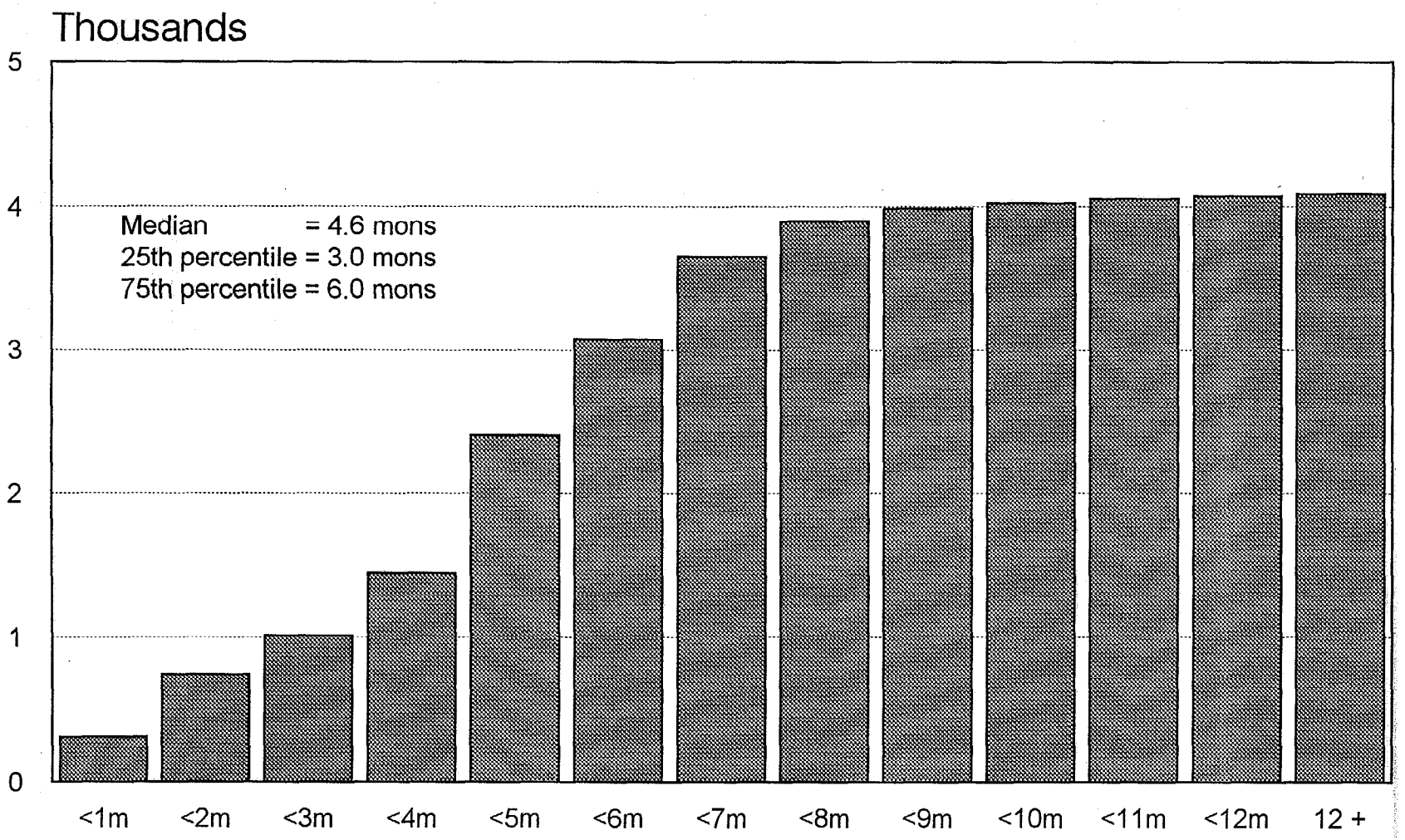
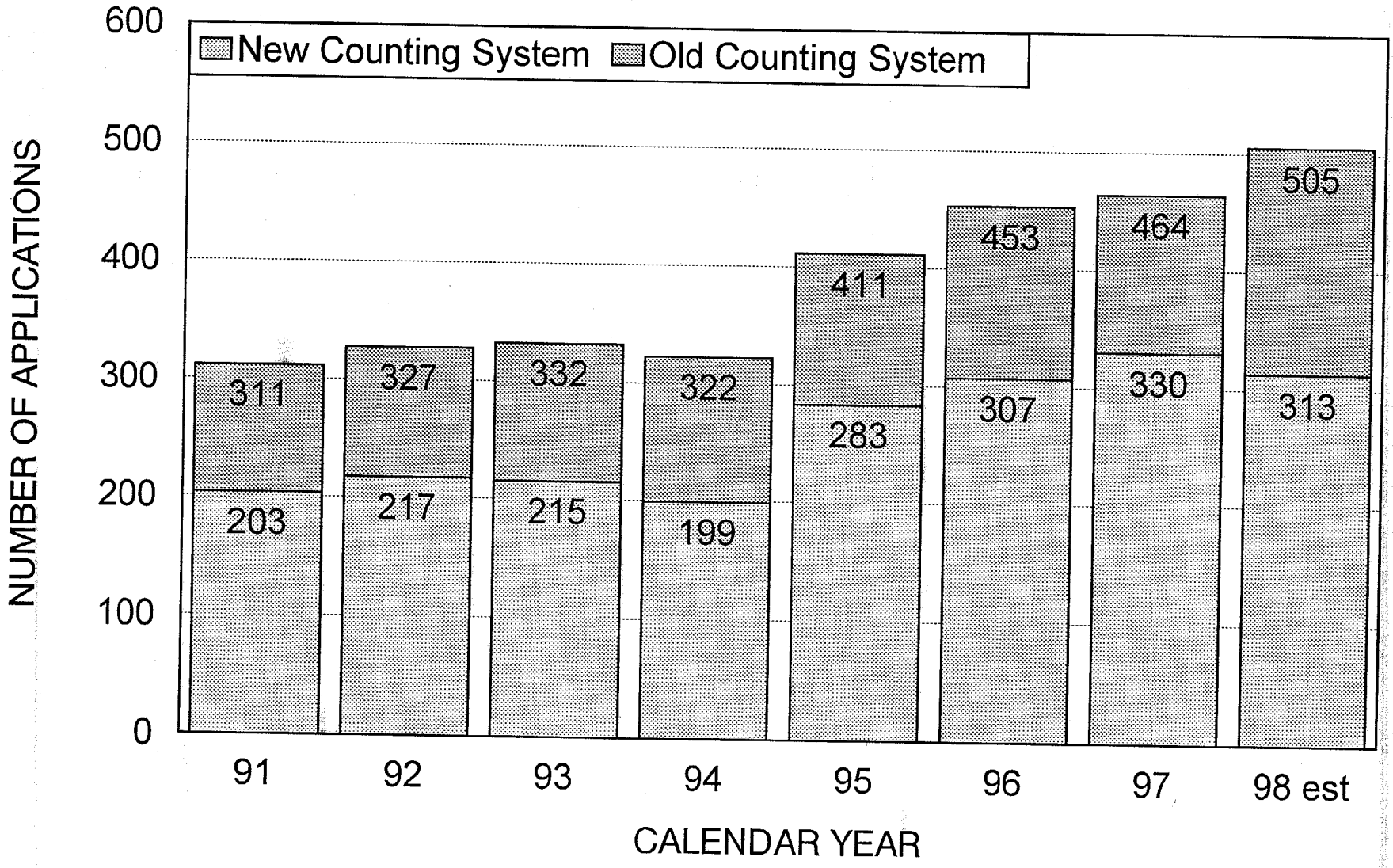
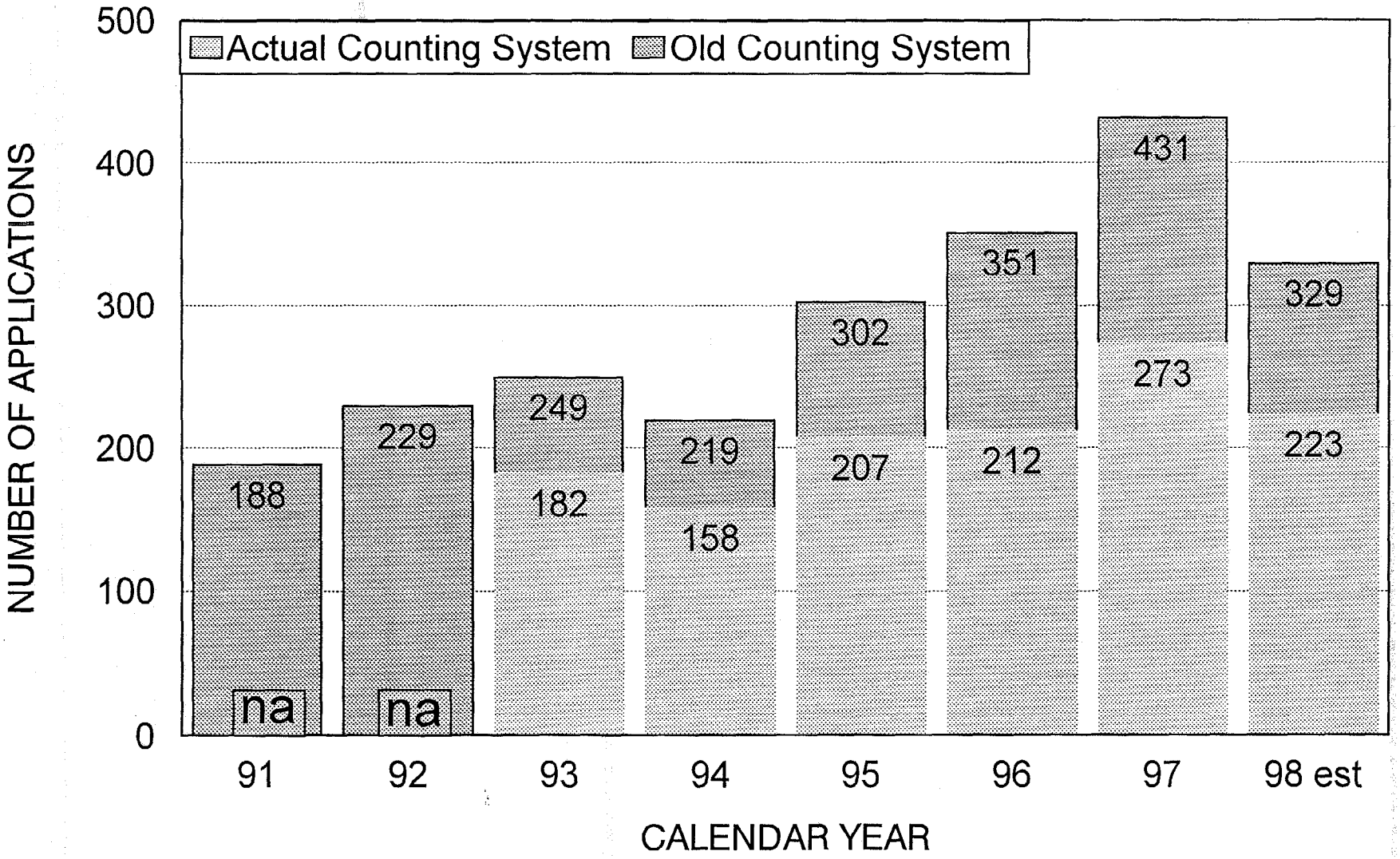
Major and Minor Cycles--1/1/97--6/30/98



Calendar Year Receipts



Calendar Year Approvals



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